REMARKS

Claims 12-27, 32-71, and 73-75 are pending in this application. Claims 1-11, 28-31, 36-55, and 72 were previously cancelled and claims 12-22 and 56-65 were previously withdrawn from consideration as drawn to a non-elected invention. By virtue of this response, claims 23 and 66 have been amended. No new matter has been added. Accordingly, claims 23-26, 32-35, 66-71, and 73-75 are currently under consideration.

With respect to all amendments and cancelled claims, Applicants have not dedicated to the public any of the subject matter of the claims as previously presented, and moreover, have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants reserve the right to pursue protection of any presently excluded claim embodiments in future continuation and/or divisional applications.

Claim Rejections Under 35 U.S.C. 112, First Paragraph

A. Claims 23-27, 32-35, 66-71, and 73-75 stand rejected under 35 U.S.C. 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the Office Action states that there is no description to support the limitation of "not transferred to the vascular system." The Examiner asserts that the passages in the specification Applicants previously cited provide support for retention in the airways and lung, but not to language excluding the vascular system.

Independent claims 23 and 66 have been amended to recite that the therapeutic agent is retained in an airway or tissue of the lung, as suggested by the Examiner. Support for this amendment is found, among other places, at page 2, lines 11-18.

In view of this amendment, withdrawal of the rejection under 35 U.S.C. 112, first paragraph is respectfully requested.

B. Claims 33-35 and 73-75 stand rejected under 35 U.S.C. 112, first paragraph for allegedly failing to reasonably provide enablement for any antihistamine. Specifically, the Office Action states that while the specification is enabling for the compounds of examples 17 and 18, it does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make any other maleimido derivative of an antihistamine. Applicants respectfully disagree.

In order to comply with the enablement requirement, the specification need not contain an example if the invention is otherwise disclosed in such a manner that one skilled in the art will be able to practice it without an undue amount of experimentation (*See* MPEP 2164.02 citing *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970)). The specification describes various reactive and linking groups on therapeutic agents, and various functional groups on the pulmonary components (*See* pp. 21-22 of the specification). Furthermore, the specification provides clear instructions regarding the methods for synthesizing a wide array of modified therapeutic agents, including antihistamines (*See* pp. 70-86 of the specification). Given this disclosure, Applicants submit that one of skill would be able to modify any antihistamine so that it will covalently bond with a fixed pulmonary component without undue experimentation.

Accordingly, withdrawal of the rejection to claims 33-35 and 73-75 under 35 U.S.C. 112, first paragraph is respectfully requested.

Claim Rejections Under 35 U.S.C. 102(b)

Claims 23-24, 26-27, 66-67, and 69-70 stand rejected under 35 U.S.C. 102(b) as being allegedly anticipated by WO 98/00171 (WO '171). Specifically, the Office Action restates Applicants' argument that WO '171 does not teach the limitation "wherein said therapeutic agent ..... is not transferred to the vascular system," and in response provides that the cited reference "teaches binding to loci which [A]pplicants disclose are stationary pulmonary components."

Independent claims 23 and 66 have been amended to recite that the modified therapeutic agent is retained in an airway or tissue of the lung. Applicants assert that the cited reference does not teach such retention. WO '171 teaches thrombin inhibitors for the treatment of thrombosis. Thrombin is a component of blood, and thrombosis is a condition in which blood clots form in blood vessels. Applicants submit that for the disclosed thrombin inhibitors to work, they must reach the target clot present in the vasculature. Thus, regardless of whether the WO '171 compounds bind to stationary pulmonary components, they are not retained in a passageway of the pulmonary system or in the lung because it is necessary for them to migrate into the vasculature to reach a site of thrombosis. For the same reason, Applicants also point out that without the amendment, binding of a modified therapeutic to a stationary pulmonary component does not teach non-transfer of the therapeutic to the vasculature.

Given that WO '171 does not teach retention of a therapeutic agent in an airway or tissue of the lung, as required by amended claims 23-24, 26-27, 66-67, and 69-70, withdrawal of the rejection under 35 U.S.C. 102(b) is respectfully requested.

Claim Rejections Under 35 U.S.C. 102(a)

Claims 23-24, 26-27, 32, 66-67, and 69-71 stand rejected under 35 U.S.C. 102(a) as allegedly being anticipated by WO 99-24462 (WO '462). In the same fashion as the above-stated rejection, the Office Action provides that WO'462 teaches binding to loci which Applicants disclose are stationary pulmonary components. Applicants again disagree that the cited reference is anticipatory.

Applicants emphasize that as amended, the claims recite that the modified therapeutic agent is retained in an airway or tissue of the lung. WO '462 (Bridon et al.) does not teach such retention. Contrary to the Examiner's conclusion, Bridon et al. describes a modified therapeutic that is transferred to the vascular system and not retained in an airway or tissue of the lung. On page 12, lines 16-23 of the Bridon et al. reference, the following is stated:

> "The subject RGD peptide derivatives will for the most part be administered parenterally, such as intravascularly (IV), intraarterially (IA), intramuscularly (IM), subcutaneously (SC), or the like. Administration may in appropriate situations be by transfusion. In some instances, where reaction of the active functional group is relatively slow, administration may be oral, nasal, rectal, transdermal or aerosol, **where the nature of the conjugate allows for transfer to the vascular system.**" (Emphasis added)

Given that Bridon et al. teaches away from retention of a modified therapeutic in an airway or tissue of the lung, withdrawal of the rejection of claims 23-24, 26-27, 32, 66-67, and 69-71 under 35 U.S.C. 102(a) is respectfully requested.

Claim Rejections Under 35 U.S.C. 103(a)

Claims 23-27, 66-70, and 23-27-27, 32-33, and 66-71 stand rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over WO '462 and WO '461 respectively in view of Edwards et al. (US 5,874,064). Specifically, the Office Action states that neither WO '462 nor WO '461 disclose dry powder inhalation but that it would have been obvious to one of ordinary skill to use the inhalation particulates of Edwards et al. in the treatments of WO '462 and WO '461 to achieve the beneficial effect of enhanced delivery. As an initial matter, Applicants assume that a typographical error has been made, and that "WO '461" is supposed to read "WO '171." Applicants request correction if this is incorrect.

Applicants disagree that the combined teachings of WO '462, WO '171, and Edwards et al. support a *prima facie* case of obviousness. "To establish a *prima facie* case of obviousness, three basic criteria must be met, one of which is that when combined, the cited references must teach or suggest all the claim limitations." *See* MPEP 2143. WO '462 and WO '171 do not teach modified therapeutics that are retained in an airway or tissue of the lung, as described in detail above. The addition of Edwards et al. was included apparently to teach dry powder inhalation. Applicants disagree with this rejection, but need not get into the details of what Edwards et al. may or may not teach or disclose. This is because Edwards et al. fails to cure the deficiency of WO '462 and WO

'171. Given that WO '462 and WO '171 have been removed as references, a *prima facie* case of obviousness cannot be established.

Accordingly, Applicants respectfully request that the rejections of claims 23-27, 66-70, and 23-27-27, 32-33, and 66-71 under 35 U.S.C. §103(a) be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 500862001810. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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